REMARKS

Status of the Claims

Claims 1, 2, and 6-10 are currently pending in this application.

Claims 1, 2 and 6-10 are amended herein. No new matter is introduced.

Objections

The Examiner has objected to the Declaration as defective because the Post Office Address and Residence of inventor Elmar Reinhold Burchardt is altered without having been initialed and dated. Applicants submit that a new Declaration is not required because 37 C.F.R. § 1.67(a)(3) provides that "[d]eficiencies or inaccuracies due to failure to meet the requirements of §1.63(c) (*e.g.*, to correct the omission of a mailing address of an inventor) in an oath or declaration may be corrected with an application data sheet in accordance with §1.76." Because the deficiency cited by the Examiner is one under §1.63(c), Applicants submit that a new Declaration is not required but rather an Applicant Data Sheet (ADS) satisfies § 1.67(a) in this instance. A new ADS setting forth the correct mailing and residential address for inventor Elmar Reinhold Burchardt is submitted herewith.

Claims 1 and 8 were objected to for failing to recite SEQ ID NOS. In response, these claims have been amended to specify that the recited sequence corresponds to "amino acids 25 to 54 of SEQ ID NO 2." Additionally, the extra period has been deleted from the end of claim 8.

Claim Rejections

35 U.S.C. §112, ¶ 1 (new matter)

Claims 8-10 stand rejected under 35 U.S.C. §112, first paragraph, because, according to the Examiner, the phrases "a sandwich immunoassay product" (claims 8-10) and "a monoclonal antibody bound to a support" (claim 8 and 9) "represent a departure from the specification and the claims as originally filed" and thus constitute new matter. Despite the fact that the specification provides extensive disclosure of immunoassays, the Examiner contends that the application as filed uses "the term immunoassay as a verb (i.e., method) not as a noun (i.e., product)." Applicants traverse this rejection.

As an initial matter, it is noted that the term "product" was included in claims 8 and 9 to clarify that those claims are directed to the physical implementations of assays rather than the methods of carrying out the assays. The term "product" is deleted from the claims by the present

amendments because the nature of the claimed subject matter is clear without this term and the amended claims more closely conform textually to the disclosure.

It is clear that Applicants were in possession of "a sandwich immunoassay" and "a monoclonal antibody bound to a support" as of the filing date of the instant application. The application describes in Example 7 the "Establishment of a PIIINP Immunoassay Based on the Recognition of Two Complementary Epitopes of the PIIINP Molecule by Two Different Monoclonal Antibodies" (p. 21, lines 20-25). The assay is said to employ "the sandwich technology" (p. 21, lines 25-26). Similarly, Example 9 describes a "PIIINP Assay on an Automated Immunoanalyzer" which was "set up as a sandwich immunoassay" (p. 23, lines 1-30). In each case, it would be readily apparent to one of ordinary skill in the art that the inventors were in possession of the physical embodiment of a "sandwich immunoassay," particularly in view of the fact that Example 9 makes reference to the fact that such an assay was "set up" -- a phrase which more commonly references a noun than a verb. The Examiner's contention that the term "immunoassay" is used only as a verb is not consistent with these disclosures which explicitly describe the physical implementations of immunoassays.

With respect to the phrase "a monoclonal antibody bound to a support," the Examiner's attention is drawn to page 11, lines 22-26 which discloses "the antibody bound to the support." The terms "support" and "capture" are used interchangeably as page 11, lines 10-16 similarly discloses "a PIIINP antibody . . . bound on a capture such as a microtiter plate." Example 8 describes such a microtiter plate coated with mAb 35J23 or mAb 35J22. Accordingly, the inventors were unambiguously in possession of "the antibody bound to the support."

Reconsideration and withdrawal of this rejection is respectfully requested.

35 U.S.C. §112, ¶ 2

Claim 2 stands rejected under 35 U.S.C. §112, first paragraph, for the recitation "characterized by preferentially binding to trimeric PIIINP" which the Examiner contends is indefinite because the "metes and bounds of such preferential binding are ambiguous and unclear." While the specifics of the Examiner's contention are not clear from the Office Action, Applicants assume that the rejection is premised on the fact that claim 2 does not explicitly recite to what the preferential binding is compared.

Applicants submit that it is clear from the specification that the antibody of claim 2 preferentially binds trimeric PIIINP as compared to monomeric Col1 domains. As explained in the application, PIIINP may be found in the serum in different molecular weight forms including intact trimeric PIIINP and "lower molecular weight species consist[ing] of monomeric Col1 domains." (p.3, lines 16-28). Assays which do not distinguish between intact (trimeric) PIIINP and degradation products (monomeric ColI domains) of PIIINP are of limited diagnostic value (p. 4, lines 12-15). In contrast, the monoclonal antibody of claim 2 has "specificity for intact PIIINP" which "further distinguishes the novel assay [using this antibody] from assays that additionally recognize lower molecular weight species" which "probably represent degradation products emanating from PIIINP and may not reflect recent collagen synthesis" (p. 22, lines 2-7). To advance prosecution of this case, claim 2 is amended herein to specify that the monoclonal antibody "is characterized by preferentially binding to trimeric PIIINP as compared to monomeric col1 domain." In view of this amendment, there can be no ambiguity about the nature of the preferential binding. Applicants respectfully submit that the rejection is overcome.

Claims 8 and 9 stand rejected as indefinite because, according to the Examiner, it is not clear which of the two recited antibodies is directed against an epitope within the 30 most N-terminal amino acids of the Col1 domain of human PIIINP. Claims 8 and 9 are amended herein to specify that the "first" antibody is a monoclonal antibody and it is this first antibody which is directed against an epitope within the 30 most N-terminal amino acids of the Col1 domain of human PIIINP. Applicants submit that this rejection is overcome.

35 U.S.C. §I12, ¶¶ I& 2 (biological deposit)

The Examiner has rejected claims 6-7 and 9 under § 112, first and second paragraphs, for being indefinite for the use of the laboratory designations "35J22" and "35J23" and for lacking enablement due to the lack of a deposit of the hybridoma.

Submitted herewith is a "Statement under 37 C.F.R. § 1.809(b)(I)" signed by the Applicant assuring the Office that acceptable deposits of the 35J22 and 35J23 cell lines, conforming to the requirements of 37 C.F.R. § 1.801-809, will be made on or before the date of payment of the issue fee.

As set forth in MPEP §2411.02, "[i]n the case that an acceptable written assurance has been made by the applicant, the rejection under 35 U.S.C. 112 directed to the absence of access

to the biological material should be removed." Accordingly, Applicants respectfully request that the § 112 rejections based on the deposit issues be withdrawn.

35 U.S.C. §103(a)

The Examiner has reiterated the rejection of claims 1-2 under 35 U.S.C. §103(a) as obvious in view of Brocks et al. (1993) *Matrix* 13:381-7 in view of U.S. Patent No. 5,512,283 (as evidenced by GenBank Accession No. P02461). Briefly, the Examiner asserts that Brocks uses epitope scanning to determine epitopes recognized by an antiserum, certain of which represented bovine amino acid sequences said to be identical to certain amino acids of the first 30 N-terminal amino acids of human PIIINP. The Examiner contends that, because binding to the Brocks epitopes was weak, it would have been obvious to use the methods described in the '283 patent to produce a monoclonal antibody against the eptiopes of procollagen taught by Brocks.

Applicants traverse this rejection on the grounds that Brocks does not teach or suggest a monoclonal antibody directed against an epitope within the 30 most N-terminal amino acids of the Col1 domain of human PIIINP. Table 1 of Brocks shows epitope scanning data for the polyclonal antibody-containing antiserum against bovine N-terminal propeptide of procollagen type lII. There is nothing in this reactivity profile that would have directed one skilled in the art to prepare a monoclonal antibody against an epitope in the range of amino acids 25 to 54 (the 30 most N-terminal amino acids of the Col1 domain). Notably, the most significant reactivity was for the pin carrying the peptide representing amino acids 142-149. There is no significant reactivity in the range of amino acids 25 to 54 that would have directed one of ordinary skill in the art to select that region for producing a monoclonal antibody. In fact, the reactivity in the range of amino acids 25 to 54 does not appear to be any greater than the reactivity against the entire sequence up to the sharp peak near residue 140. Therefore, there is nothing to differentiate this region or to recommend forming a monoclonal antibody against it. The contention that Brocks would have motivated one skilled in the art to make a monoclonal antibody directed against an epitope within the range of amino acids 25 to 54 (the 30 most N-terminal amino acids of the Col1 domain) is impermissibly based on hindsight.

Applicants respectfully request reconsideration and withdrawal of the rejection over Brocks.

CONCLUSION

Applicants respectfully submit that the instant application is in condition for allowance. Entry of the amendments and an action passing this case to issue is therefore respectfully requested. In the event that a telephone conference would facilitate examination of this application in any way, the Examiner is invited to contact the undersigned at the number provided.

AUTHORIZATION

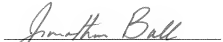
The Commissioner is hereby authorized to charge any fees which may be required for this amendment, or credit any overpayment to Deposit Account No. **50-3732**, Order No. **14173.105005**. Furthermore, in the event that an extension of time is required, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to the above-noted Deposit Account No. **50-3732** and Order No. **14173.105005**.

Respectfully submitted,

KING & SPALDING, L.L.P.

Dated: March 27, 2008

By:



Jonathan D. Ball

Registration No. 59,928

Mailing Address:

KING & SPALDING, L.L.P.
1185 Avenue of the Americas
New York, New York 10036-4003
(212) 556-2115
(212) 556-2222 (Fax)